SURGERY FOR CORONARY ARTERY DISEASE PLACED IN PERSPECTIVE*

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THE subject of this symposium is a surgical procedure which may turn out to be the most significant advance in the therapy of heart disease in our time. This procedure represents a simple, direct mechanical approach to the problem of coronary artery obstruction and hence to the most important cardiac cause of death and disability. There is a climate of enthusiasm and optimism throughout the world which has extended from the medical community through the press to the lay population. Patients now make the diagnosis and seek a surgeon to treat the disease.

There are good reasons to be optimistic about this procedure, and I am optimistic, but this optimism must be tempered by knowledge of the past history of surgical therapy for ischemic heart disease, which has been characterized by periods of enthusiasm followed by deep disappointment. We must remember that glowing reports have followed the introduction of pericardial poudrage, internal mammary ligation, and internal mammary implantation. The current procedure should be better than its predecessor, but its superiority must be proved.

First I address myself to my title and attempt to place surgery for coronary artery disease in the proper perspective. This will require some review of available data on the natural history of ischemic heart disease both with and without therapy. It also will be necessary for me to review experience with other surgical procedures. This will lead naturally to a discussion of the problem of evaluation of the results of surgery. Finally, I shall tell you what we at the Johns Hopkins Hospital in Baltimore are actually doing with regard to the selection of patients for surgery.

Dr. Harry Kemp incorporated in the title the words "Placed in Per-

*Presented as part of a *Conference on Myocardial Revascularization* held by the New York Heart Association at The Waldorf-Astoria, New York, N. Y., January 25, 1972.

spective" and, as I think about the meaning of the word perspective, I realize that the addition is appropriate. Perspective is defined as the appearance to the eye of objects in respect to their relative distances and positions. How you see the picture depends on a number of factors: for example, on who you are and what your viewpoint is. If you are a surgeon, you will see the picture from one point of view; the pathologist and epidemiologist have other viewpoints. The surgeon sees the operative candidate and the good results, but does not have similar exposure to the patients who are treated medically. The pathologist sees the bad results and his view is colored by his closer contact with surgical failures. The view of the subject also depends on the time. What we have seen in 1971 will not be the same as what we shall see in 1972 and 1973 —this is historical perspective.

Placed in Perspective

The first step in placing coronary surgery in perspective is to present what might be called the big picture of ischemic heart disease. In Figure 1 the background information against which we must view the surgical procedure is presented. The various presentations or stages in the evolution of ischemic heart disease are shown as boxes or circles. The large population of patients with asymptomatic coronary atherosclerosis is indicated by the circle at the left. Asymptomatic coronary atherosclerosis becomes symptomatic ischemic heart disease in a number of ways, as indicated by the arrows leading to the right. The patient may become symptomatic by presenting with angina pectoris or with a myocardial infarction, or he may die suddenly.

The rate constants are approximations derived from part of the *Framingham Study* and indicate that the rate of movement from asymptomatic to symptomatic is approximately 1% per year; half the patients becoming symptomatic do so with a myocardial infarction.[1] A third present with angina pectoris and a fifth with sudden death. Flow between these groups is also possible, as indicated by the arrows.

In Figure 2 we have enlarged a segment of Figure 1 and added another presentation, referred to as the intermediate syndromes. We prefer the term "intermediate syndrome" to describe a group of conditions which include unstable angina pectoris and angina at rest. We no not utilize the term "preinfarction" for these conditions as this term implies knowledge of the future, which we do not have. I think that the im-

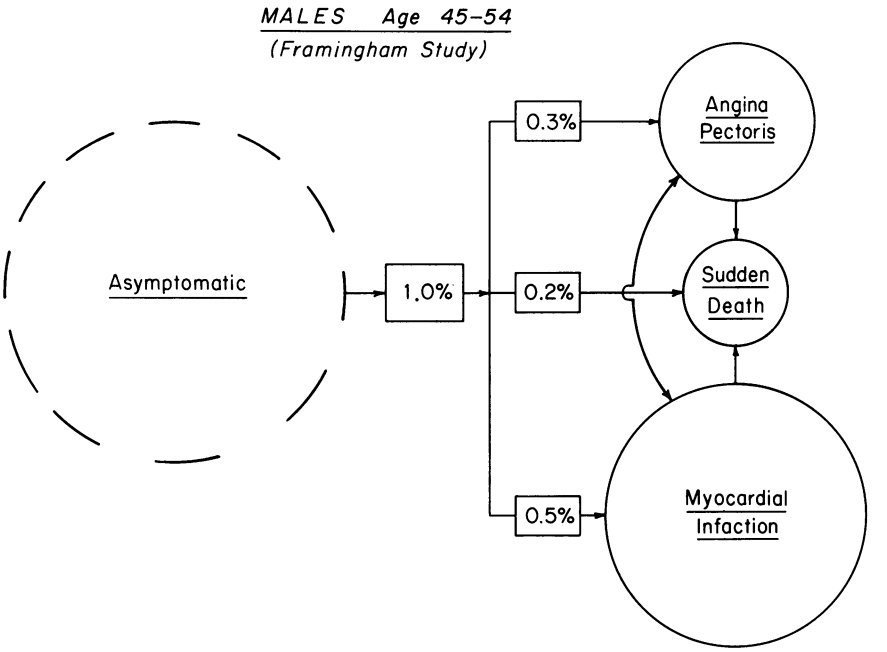

Fig. 1. Presentation of ischemic heart disease.

proper use of the term "preinfarction" represents one of the major problems we have in the evaluation of results at the present time. Here again, we can come back to the title or theme of this contribution and point out that whether a given condition is preinfarction or not depends on the perspective. If the patient has had an infarction, it is easy to identify the symptoms he had last week as preinfarction, and such a retrospective investigation indicates that more than half the patients with myocardial infarction had some form of illness during the two weeks prior to their infarct.[2] It is far less easy to identify the preinfarction state from the other end of the system. For example, Fulton in Edinburgh, working with Oliver and Julian, conducted a prospective community survey utilizing the general practitioners in Edinburgh, Scotland.[3] These investigators identified 100 patients with unstable angina, which would fall into our intermediate syndrome group, and of this group three died suddenly and 15 developed acute myocardial infarction within three months of identification. Accordingly there was an incidence of 18% of either sudden death or acute myocardial infarc-

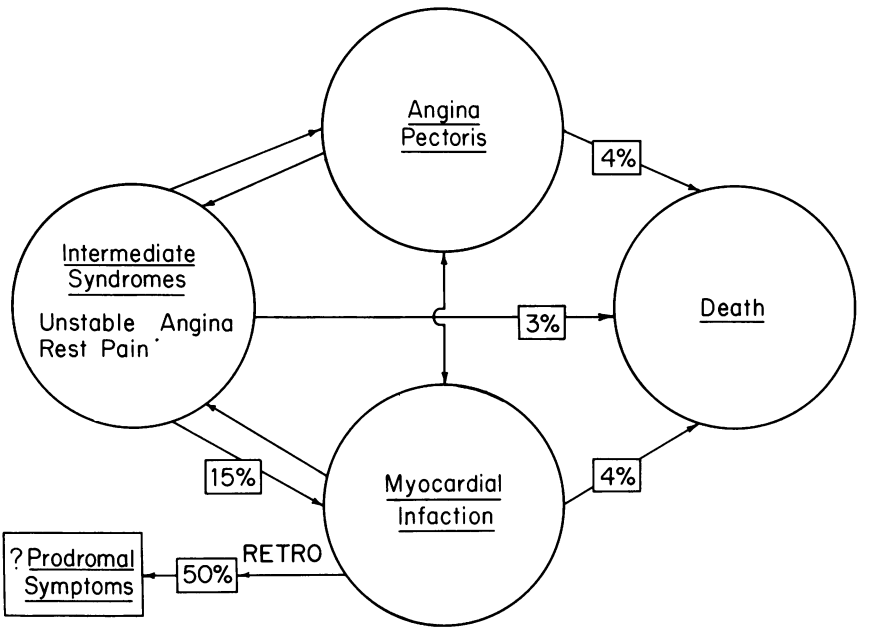

Fig. 2. Interrelation between clinical presentations of ischemic heart disease.

tion in patients identified prospectively as potentially preinfarction. This is to be contrasted with figures obtained retrospectively, which often exceed 50%.

Another point to be made from Figure 2 is that each large circle contains many subsets. For example, within a group clinically defined as having angina pectoris, there are high-risk groups and low-risk groups which can be identified on the basis of clinical presentation, arteriographic pattern, or a combination of the two. Frank has done this in the study made by the Health Insurance Plan of Greater New York (HIP).[4] He has shown that the angina group has an over-all mortality rate of 4% per year, but on the basis of the electrocardiogram and blood pressure it is possible to split this group into two subsets. The high-risk group has a mortality of 8% per year and the low-risk group a mortality of 2% per year, which is very close to the expected mortality of an asymptomatic population.

We believe it is possible to refine this categorization of patients further by means of coronary arteriography (Figure 3). For example,

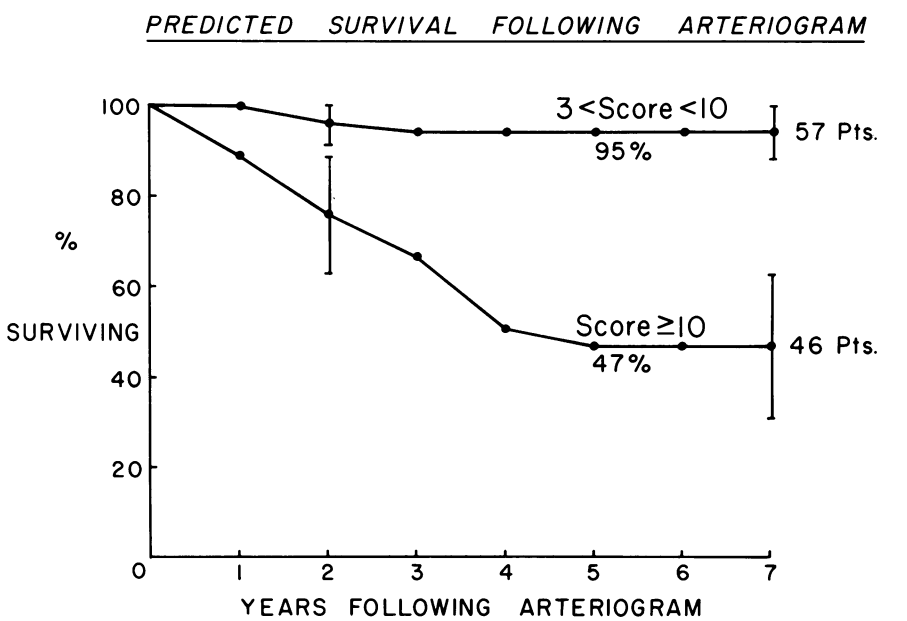

Fig. 3. Prognostic significance of coronary arteriography. The scoring system is based upon five points for each of three vessels, the maximum score being 15.

utilizing a scoring system for the entire vascular tree of 0 to 15 it is possible to identify a group with scores of 10 or above who have a mortality rate of 10% per year as opposed to a group with scores between 3 and 10 who have a mortality rate of 0.4% per year. Thus on the basis of arteriography it is possible to identify groups with a 50% probability of death in five years and another group with a 2% risk in the same period of time.[5] This 25-fold variation in the prognosis within a clinically defined group of angina patients makes it essential that any attempt to evaluate the effect of operation on mortality should be based upon a comparison of arteriographically comparable groups.

Lessons of the Past

Now I should like to turn to the past history of coronary-artery operations. This consideration of the lessons of the past is essential if the aortocoronary bypass is to be placed in proper perspective. I ask you to recall the excellent studies of Cobb and Dimond performed in 1959 and 1960.[6, 7] These authors were attempting to evaluate the then popular

internal mammary-ligation operation. Patients were selected for the procedure on the basis of precise criteria and then taken to the operating room where the internal mammary artery was isolated by the surgeon. At this point a card was drawn which instructed the surgeon either to close the incision or ligate the vessel and then close the incision. The surgical procedures were carried out in such a way that the cardiologist responsible for the postoperative evaluation was unaware of which procedure was done.

The results of these similar studies can be combined and, when this is done, the results show that 12 of 17 patients who had the sham procedure consisting only of a skin incision experienced subjective improvement, and two of the nine patients had objective evidence of improved exercise tolerance. Similar changes were noted in the group in which the internal mammary artery was ligated; hence this operation was judged to be of no value. This experience of L. A. Cobb and E. G. Dimond, working independently in two different centers, focused attention on the placebo effect of any surgical procedure in patients with angina pectoris.

Next in the review of past history I call attention to the 1968 paper of Björk.[8] The pertinent results of this study, which is one of the best of many studies designed to evaluate the internal mammary-implant operation, are summarized in Table I. Björk studied 56 patients who had a Beck-Vineberg procedure (BV), which is in essence a Vineberg procedure or an internal mammary-implant operation carried out in conjunction with a Beck procedure or pericardial poudrage. As a control series he used a group of patients who had been studied in a similar way but treated with the Beck operation during the preceding period of several years. These data show that 75% of the patients who had the Beck procedure experienced subjective improvement as compared to 77% of those who had the Beck-Vineberg procedure. Exercise tolerance as measured on the bicycle ergometer was increased in 61% and 58% respectively. The mortality in the first year following operation, the primary postoperative period excluded, was 6.5% and 8% respectively. There is obviously no significant difference between these two operative procedures with regard to subjective improvement, exercise tolerance, or mortality.

The third column in Table I refers to the patency of the internal mammary artery at the time of restudy; it applies, therefore, only to

TABLE I. THE BECK (B) OPERATION VERSUS THE BECK-VINEBERG (BV) OPERATION*

	B (84)	*BV (56)*	*IMA*
Subjective improvement	75%	77%	50%
Exercise tolerance increase	61%	58%	50%
Mortality first year Primary period excluded	6.5%	8.0%	

*Data from Björck, L. et al.[8]

the Beck-Vineberg series. It is highly significant that only 50% of the group which was subjectively improved had patent vessels; similarly only 50% of the patients who had improved exercise tolerance had patent and functional implants. Conversely, 50% of the vessels were occluded. These results could be interpreted as showing that either the pericardial poudrage is the important part of the Beck-Vineberg or that the placebo effect of operation is responsible for an improvement in both groups.

In view of these and other reports evaluating the Beck-Vineberg procedure it is surprising that this operation is still being recommended in some centers as an adjunct to the vein-bypass procedure or as a procedure which can be used when the situation is not suitable for vein bypass.

The purpose of this review of past experience is not to condemn or recommend the Beck procedure, the ligation of the internal mammary artery, or its implantation into the myocardium, but to call attention to the placebo effect of operation in all patients, especially in those with angina pectoris. I commend to you Henry Beecher's essay, *Surgery as a Placebo*, which was presented as part of the 150th Anniversary of the Massachusetts General Hosptial in 1961.[9] Beecher makes several excellent points about the placebo effect of surgery. First, the magnitude of the placebo effect is directly related to the emotional stress associated with the illness. Second, he showed that the magnitude of the placebo effect is related to the enthusiasm of the surgeon. Beecher also points out that the 35% of patients experiencing improvement following a placebo operation is roughly the same as the fraction deriving benefit from a placebo medication.

I leave the placebo effect with a quote from Wolfe, who says, "The degree to which (the physician) is able to induce in his patients a state of arousal or readiness for a favorable response, the more potent the medication he gives will be. In other words, placebo effects are potent where there is strong motivation on the part of the patient toward recovery." What stronger motivation could there be than prevention of the widely publicized and much feared heart attack with the potential for sudden death?

Evaluation of Results

If it were easy to evaluate the results of the aortocoronary bypass procedure, this subject would not have been selected for this conference. The importance of the problem has been recognized nationally by the appointment of committees to study the problem and make recommendations. It has also resulted in a flood of editorials, some of which have ingenious titles which give some idea of their content.[10-15] One of the most revealing titles is that of Spodick in the *American Heart Journal* one year ago: "Revascularization of the Heart—Numerators in Search of Denominators."[16] Another title worthy of remembrance was selected by Braunwald: "A Plea not to let the Genie out of the Bottle."[17]

The evaluation of this promising new operative procedure is difficult for many reasons. We have already referred to the placebo effect of the operation which, as Beecher pointed out, is heightened by emotional stress. All physicians feel frustrated by seeing ischemic heart disease limit the productive years of life. We are optimistic about the operation and appropriately convey this optimism to our patients; by so doing we make the task of evaluation more difficult. We all hope that we can alter the natural history by this operative procedure. The physician is thinking not only of his patients but often of himself, recognizing that he is a prime candidate for ischemic heart disease.

There are also economic factors at work which make it difficult to be objective. There are cardiac surgical teams in hospitals in this country which have been doing only an occasional case—one to two per week—who now, for the first time, see an opportunity to utilize the equipment and personnel and fully to profit economically from them.

There are three major criteria upon which the new operative procedure should be judged as set forth in Table II. Quite properly, symp-

TABLE II. CRITERIA FOR EVALUATION OF THE VEIN-BYPASS OPERATION

1) Symptomatic improvement
2) Functional capacity improved
   a) Exercise capacity
   b) Ventricular function
3) Natural history improved
   a) Death
   b) Myocardial infarction

tomatic improvement should be put first in this list because the patient comes to the physician with a symptom which requires relief. The current experience with vein-bypass operations indicates that relief can be expected in 85% of patients. Improvement in the quality of life has been emphasized as a major argument for operation and is certainly a worthy objective for any therapeutic procedure, and should not be depreciated. If improvement in the quality of life by relief of symptoms were the only objective, surgical therapy should be compared to medical therapy with respect to effectiveness, safety, and cost. There are many studies which indicate that improvement in the quality of life of patients with angina pectoris can be expected in from 65 to 95% of patients with a variety of therapeutic agents. We recognize relief of symptoms as an important objective in the treatment of angina pectoris, but we point out that because of the placebo effect of both medical and surgical therapy in this group of patients symptomatic improvement cannot be taken as evidence that a fundamental change in the disease process has been effected. Our enthusiasm for operation is not based on the ability of the operation to relieve symptoms; we must expect more of operations than just symptomatic improvement and, therefore, we must not judge the operation solely on this basis.

The second criterion is improvement in functional capacity. This can be measured in terms of capacity for exercise or by direct measurement of ventricular function. Numerous studies of both varieties have been reported in the last few months, and all are encouraging.[18, 19] However, a word of caution is in order with regard to the interpretation of improved exercise tolerance. I believe the data available indicate that there is a significant psychological effect on exercise tolerance. You will recall that improved exercise tolerance was noted in a significant num-

TABLE III. DEATHS FROM ALL CAUSES AMONG MALES*

Total group	18%	4.0%
High-risk		
Abnormal ECG and BP	36%	8.0%
Low-risk		
Normal ECG and BP	8%	1.8%
No coronary heart disease	5%	1.1%

*Data from study conducted by the Health Insurance Plan of Greater New York. Frank, C. W.[4]

ber of patients subjected to sham operations or with occluded internal-mammary implants. The end point for the exercise test is at least in part subjective.

Measurements of ventricular function have also yielded encouraging results. Several studies have shown disappearance of areas of akinesis and improvement in hemodynamic response to stress.[20-23] Intuitively we reason that this improvement has followed the operation and therefore has occurred because the operation has improved the blood supply to the myocardium. *Post hoc ergo propter hoc*—a well known trap. This may be so, but here again we must remember that there *are* no controls. Accordingly there is an alternative possibility which we cannot rule out with existing data. The alternative possibility is that the improvement represents the result of spontaneous variation in the course of the disease or possibly a nonspecific effect of an operation explained by loss of weight, improved medical therapy, or the neurohormonal response to surgery.

The third criterion is improvement in natural history. At this point, let us remember that it is the effect which we, as physicians and surgeons, and our patients hope we are obtaining. Symptomatic improvement is important, but if it were our only objective we would not turn to surgery. We anticipate that surgery is doing more than relieving symptoms. The current enthusiasm is based upon the hope that the operation is reducing the probability of sudden death and myocardial infarction.

The determination of the effect on natural history is not an easy problem because the untreated natural history is so variable. The surgical group must be compared to a comparable medical group. Frank, in

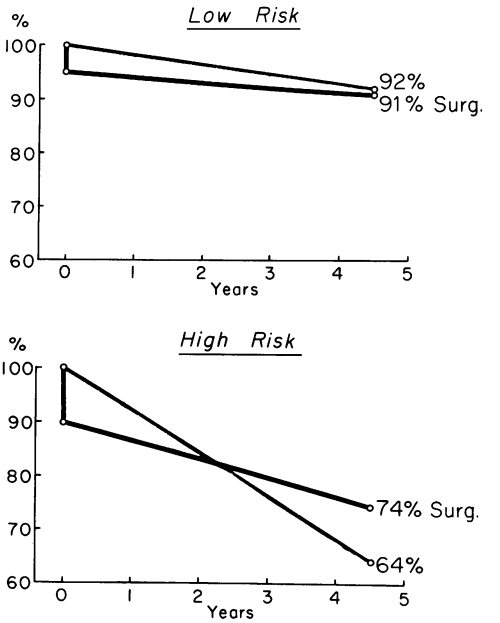

Fig. 4. Hypothetical life table showing possible effect of operation on a low-risk and a high-risk population.

reporting on the HIP, has demonstrated that it is possible to identify high-risk and low-risk groups on the basis of clinical classification.[4] As indicated in Table III, the over-all probability of death in four and one half years is 18% for men, but this group can be divided into a high-risk group (patients with an abnormal ECG and blood pressure) with a probability of 36% and a low-risk group (patients with normal ECG and blood pressure) with a probability of 8%. The 8% figure is not very different from the 5% reported for the general population of the same age and sex. Arteriography is a helpful adjunct in this regard as it enables us to break down clinical groups of patients into subsets with a more clearly defined mortality rate (Figure 3).[6] The more precisely we can identfy the rate constant, the smaller will be the damage which can be detected.

The problem of evaluating the effect of surgical therapy on natural history is illustrated in Figure 4. In the first panel are shown the five-year survival curves of two populations of patients with ischemic heart

disease, identified by Frank as the high-risk group and the low-risk group. The high-risk group has an expected mortality of 36% in four and one half years, and the low-risk group has a mortality of 8% in the same period. If the effect of the vein-bypass operation is to be observed on the low-risk group, the situation is as depicted in the upper graph. The mortality rate has been cut in half from 8% to 4%, but we have accepted a 5% operative mortality rate at the outset, so even with the lesser rate it will take four and one half years for the two lines to meet and more than five years before significant differences will become apparent.

Let us now examine the situation which exists with the more severely ill population in the bottom graph. You will note that here again the mortality rate has been cut in half from 36% to 18% in 4.5 years, but the operative mortality is higher and has been assumed to be twice that in the mild group. It again takes two years for the mortality lines to cross and five years for the differences to become significant.

The problem of establishing an effect on natural history is not, therefore, an easy one. Ideally, as D. H. Spodick, Chalmers, and others have pointed out, a study of the effect on natural history should be carried out prospectively with the random allocation of cases into surgical and nonsurgical groups.[16, 24] This is difficult and possibly impossible, but it is being attempted by several groups around the world.

A less good but possibly acceptable alternative is to identify surgical and medical groups which are comparable on the basis of arteriographic anatomy. If the results are good, by which I mean if the mortality rate is cut in half or better and the operative mortality is low, an answer may be obtained. If, on the other hand, the differences are smaller, they may be apparent only if a random prospective trial is completed.

We have talked mostly about the natural history of the unoperated population, but many important questions remain to be answered about the operated population. It is important to recognize that the natural history of the treated population is not that of the normal population. I think some physicians and surgeons forget that the bypassing of a single obstructing lesion does not restore the patient to the population of normals. This is true for a number of reasons: first and foremost, the basic underlying atherosclerotic disease process in the coronary vessels continues and, indeed, there may be progression of the changes in the native circulation. If the patient has sustained a myocardial infarction

TABLE IV. FACTORS INFLUENCING FATE OF OPERATED POPULATION

1)	Fate of the vein
	Internal fibrous proliferation
	State of peripheral vessels
2)	Fate of native coronary circulation
3)	Incidence of postoperative myocardial infarction

in the past, this of course will still be present with all the consequences thereof.

Some of these critical questions about the future of the operated population are listed in Table IV. We must consider the natural history of the implanted vein. We are comparing the probability of future patency of the implanted vein with the probability of future patency of the native circulation. First and foremost is concern with the fate of the vein itself. There are now reports of patency at one to two years after operation from 60% to 80%. There are also histologic studies of the veins from the 20% to 40% which are occluded. These veins show an intimal fibrous proliferation which has been recognized for many years as a change which occurs when a vein is exposed to arterial pressure. The experience with the use of saphenous veins in the lower extremity is relevant and worth considering. Baddeley showed a progressive decrease in the patency of veins as time passed after operation. He showed that the patency rate fell progressively with time from 79% at one year to 61% in five years.[25] He also emphasized the importance of distal run-off and hence the state of peripheral vessels in determining the probability of long-term patency.

The second question concerns the effect of the grafting procedure on the native circulation. This is closely related to the third question, which has to do with the incidence of postoperative infarction. Several centers estimate the incidence of myocardial infarction in the postoperative period to be 25%. The diagnosis of infarction was established by change in the electrocardiogram associated with evidence of thrombosis of a segment of the native circulation at the time of postoperative arteriographic study.[26, 27]

CURRENT PRACTICE

Now I turn to the final topic and shall attempt to tell you what we

TABLE V. INDICATIONS FOR VEIN-BYPASS GRAFT OPERATION
(January 1972)

	Indicated	*Individual decision*	*Not indicated*
Symptomatic presentation	Stable angina pectoris	Unstable angina pectoris	Asymptomatic
Angiographic pattern	Combination of proximal lesions	Single proximal lesion	Diffuse disease or single lesion 50% or less
Ventricular function	Good or single area of dysfuntcion	Multiple areas of dysfunction	Generalized dysfunction

are actually doing at Johns Hopkins University at the present time. We feel that the selection of patients for vein-bypass operation depends upon three factors: 1) symptomatic presentation; 2) arteriographic anatomy; and 3) ventricular function. If we were sure that the operation were capable of altering the natural history, we should be willing to advise operation on the basis of the arteriographic anatomy and ventricular function alone. This is not, however, the case, and therefore we utilize all three factors in arriving at our decision. The criteria are not rigid and there is room for flexibility and individualization. The principles of selection, however, are outlined in Table V.

The population of candidates is divided according to symtomatic presentation, arteriographic pattern, and ventricular function. The three columns describe our current practice concerning the indications for surgical therapy. The column at far left describes a group of patients for which operations are indicated, and the column at the far right a group for which the procedure is not indicated; the middle describes an uncertain group. Combinations are possible; for example, we occasionally operate upon an asymptomatic patient if arteriographic anatomy and ventricular function are ideal. We may also in an individual case advise an operation for a patient with poor ventricular function if all the other factors are suitable. It is clear, however, that the state of ventricular function is the single most important factor in determining operative mortality.

The indications change from month to month as more information is obtained. I think all would agree that there is no way at present to predict what the indications will be five years from now. We must not

allow wishful thinking to render us incapable of critical evaluation of results.

Summary

Surgical therapy for coronary disease can be placed in perspective in 1972 by listing certain facts which are known about the aortocoronary-bypass operation and preparing another list of important unknowns. First, the known facts:

1) The operative mortality ranges from approximately 3% to 10%. Ventricular function is an important determinant of operative mortality. The more severe the impairment of function, the higher the mortality.

2) The flow through the grafts is significant, with measurements ranging from 30 to 90 ml./min.

3) The patency rate at two years varies from 60 to 80%.

4) Symptomatic improvement can be expected in 85% of patients.

5) Objective evidence of improved exercise tolerance can be expected in 85% of patients.

The unknowns at this time are:

1) The effect of the operative procedure on the natural history of the disease as manifested by the incidence of death and myocardial infarction.

2) The incidence of postoperative myocardial infarctions.

3) The fate of the vein graft.

4) The fate of the native circulation.

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